

PCTWORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : A01N 65/00	A1	(11) International Publication Number: WO 98/41096 (43) International Publication Date: 24 September 1998 (24.09.98)
(21) International Application Number: PCT/US98/05494 (22) International Filing Date: 19 March 1998 (19.03.98) (30) Priority Data: 60/042,540 19 March 1997 (19.03.97) US (71)(72) Applicant and Inventor: D'JANG, Arthur, H., K. [US/US]; 13961 Sisson Highway, Collins, NY 14034 (US). (74) Agents: KADLE, Ranjana et al.; Hodgson, Russ, Andrews, Woods & Goodyear, 1800 One M & T Plaza, Buffalo, NY 14203-2391 (US).		(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i>
(54) Title: HERBAL EXTRACT COMPOSITION AND METHOD OF MAKING THE SAME (57) Abstract Provided is a herbal extract-based composition comprising an extract of Gynostemma pentaphyllum, an extract of Crataegus pinnatifidia (hawthorn leaves or berries), and an extract of Camellia Sinensis (green tea). Also provided is a process for preparing a herbal extract-based composition which comprises separately extracting each of hawthorn berries, green tea leaves, and Gynostemma pentaphyllum leaves; drying extraction eluates obtained from the extracting of each of hawthorn berries, green tea leaves, and Gynostemma pentaphyllum leaves to obtain organic residues in forming a hawthorn berry extract powder, green tea extract powder, and a Gynostemma pentaphyllum extract powder; and combining the green tea extract powder, the Gynostemma pentaphyllum extract powder, and the hawthorn berry extract powder in desired proportions to form the herbal extract-based composition which has health promoting effects including potent inhibition of free radicals.		

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece	ML	Mali	TR	Turkey
BG	Bulgaria	HU	Hungary	MN	Mongolia	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MR	Mauritania	UA	Ukraine
BR	Brazil	IL	Israel	MW	Malawi	UG	Uganda
BY	Belarus	IS	Iceland	MX	Mexico	US	United States of America
CA	Canada	IT	Italy	NE	Niger	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NL	Netherlands	VN	Viet Nam
CG	Congo	KE	Kenya	NO	Norway	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NZ	New Zealand	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	PL	Poland		
CM	Cameroon	KR	Republic of Korea	PT	Portugal		
CN	China	KZ	Kazakstan	RO	Romania		
CU	Cuba	LC	Saint Lucia	RU	Russian Federation		
CZ	Czech Republic	LI	Liechtenstein	SD	Sudan		
DE	Germany	LK	Sri Lanka	SE	Sweden		
DK	Denmark	LR	Liberia	SG	Singapore		
EE	Estonia						

HERBAL EXTRACT COMPOSITION AND METHOD OF MAKING THE SAME

This application claims priority of earlier filed provisional application serial number 60/042,540, filed on March 19, 1997, which is incorporated herein by this reference.

5

Field of the Invention

The present invention relates to an herbal extract-based composition comprised of a combination of three components: an extract of *Gynostemma pentaphyllum*, an
10 extract of *Crataegus pinnatifidia*, and an extract of *Camellia sinensis*. The present invention also provides a method of making the composition for therapeutic uses, and as a dietary supplement for promoting health.

15 **Background of the Invention**

Generally, herbal supplements are natural, safe when taken as recommended, and less expensive and sometimes more effective alternatives to drugs. These plant-based pharmaceuticals are used for medicinal
20 purposes; and/or dietary supplements for disease prevention, for relief of ailments, and for health maintenance (collectively "health promoting"). *Gynostemma pentaphyllum*, *Crataegus pinnatifidia*, and *Camellia sinensis* have been used individually for
25 particular therapeutic applications.

1. *Gynostemma pentaphyllum*

Gynostemma pentaphyllum, also known as 5-leaf ginseng or jiaogulan or southern ginseng, is from the
30 cucumber family and has traditionally been grown in a mountainous region in South Central China. This herb, a completely different plant than ginseng, is rich in special saponins termed "gypenosides" which are similar, and some identical, to the ginsenosides found in
35 ginseng, but at a level several fold higher. These saponins have been shown to have antioxidant/cell

protective effects. More particularly, the saponins protected cell membranes and cytosols, from oxidative injury, neutralize free radicals, helped preserve immune function during irradiation, lowered blood pressure, reduced vascular resistance, effects anti-platelet-aggregation, and reduced levels of serum triglycerides and total cholesterol (Gormley et al., 1997, *Better Nutrition* 59:42).

10 2. *Crataegus pinnatifidia*

 The leaves and berries of *Crataegus pinnatifidia*, also known as hawthorn, have been used traditionally for the treatment of heart conditions and for cardiovascular health. The hawthorn fruits (berries), known as
15 "Shan-zha, have been used to improve digestion, and to alleviate various stomach ailments. Saponins, flavonoids (including hyperoside), and anthocyanins (including proanthocyanidins) extracted from hawthorn fruits have also shown cardiogenic (heart stimulating
20 and regulating) activity including inhibition of arrhythmia, normalization of blood pressure, dilation of blood vessels and increase in coronary blood flow, reduction of serum triglyceride and cholesterol levels, reduction in symptoms of angina, and improvement of
25 circulation (Foster, 1997, *Better Nutrition*, 59:56; Foster, 1989, *Bestways* 17:46; McCaleb, 1991, *Better Nutrition for Today's Living* 53:32).

 3. *Camellia sinensis*

30 Dried leaves from the *Camellia sinensis* plant is processed into three types of tea: oolong tea, black tea, and green tea. In making green tea, the tea leaves are stabilized by moist or dry heat which destroys the enzyme polyphenoloxidase and thus, prevents oxidation of
35 polyphenols. These polyphenols are the main biologically active ingredients in green tea. Catechins,

a chemical group of polyphenols possessing antioxidant properties (protects cells from free radical-mediated damage), include epigallocatechin-3 gallate (ECGC), epigallocatechin, and epicatechin-3-gallate. Recently, ECGC has been shown to be an inhibitor of urokinase, and enzyme crucial for cancer growth (Jankun et al., 1997, *Nature* 387:561). The polyphenols in green tea, accounting for as much as 40% of tea's dry solids, have also been shown to reduce serum cholesterol and LDL (low density lipoprotein). Green tea polyphenols have been shown to prevent microbial (bacterial and viral) infections. For example, green tea polyphenols damage bacterial membranes (Dolby, 1997, *Better Nutrition*, 59:22). Further, extracts of green tea have been shown to prevent cancers of the lung, breast, prostate, liver, skin, esophagus, and colon. Green tea is also high in cavity-fighting fluoride the amount of tea used to prepare one cup has approximately 0.3 milligrams of fluoride.

While *Gynostemma pentaphyllum*, *Crataegus pinnatifidia*, and *Camellia sinensis* have been used individually for health promoting and therapeutic purposes, not described is the arrangement and composition comprising an extract of *Gynostemma pentaphyllum*, an extract of *Crataegus pinnatifidia* (hawthorn berries or leaves) and an extract of *Camellia sinensis* (green tea) for health promoting and therapeutic uses.

Summary of the Invention

This invention relates to a herbal extract-based composition that comprises about 10 to about 30 percent by weight of *Gynostemma pentaphyllum* extract, about 10 to about 30 percent by weight of green tea extract, and about 40 to about 75 percent by weight of hawthorn berries extract. Preferably, the herbal extract-based

composition comprises about 20 percent by weight of Gynostemma pentaphyllum extract, about 20 percent by weight of green tea extract, and about 60 percent by weight of hawthorn berries extract.

5 Another aspect of the present invention is a process for preparing the herbal extract-based composition. Essentially, this method comprises separately extracting each herbal component (hawthorn berries, green tea leaves, and leaves of Gynostemma
10 pentaphyllum); drying the extraction eluates to obtain the organic residues in forming a hawthorn berry extract powder, green tea extract powder, and a Gynostemma pentaphyllum extract powder; and combining the green tea extract powder, the Gynostemma pentaphyllum extract
15 powder, and the hawthorn berry extract powder in desired proportions to form the herbal extract-based composition. In one embodiment, this method comprises the steps of:

- 20 (a) separately extracting a first batch of macerated hawthorn berries, cut green tea leaves, and cut Gynostemma pentaphyllum leaves in warm (greater than room temperature) water;
- (b) recovering a first extract eluate from the respective extraction of each herbal component;
- 25 (c) repeating step (a), recovering a second extract eluate and pooling the first and second extract eluates of the respective herbal component;
- (d) separately extract a second batch of macerated hawthorn berries, cut green tea leaves, and cut
30 Gynostemma pentaphyllum leaves in an aqueous alcohol (e.g., 70% ethanol);
- (e) recovering a first aqueous alcohol extract eluate from the respective aqueous alcohol extraction of each herbal component;
- 35 (f) repeating step (d), recovering a second aqueous alcohol extract eluate from the respective aqueous

- 5 -

alcohol extraction of each herbal component, and pooling the second aqueous alcohol extract eluate with the respective first aqueous alcohol extract eluate from each herbal component;

- 5 (g) recovering the organic residue of each herbal component by reducing the liquid portion of each of the respective pooled eluates by drying (air drying, freeze drying or a combination thereof), in forming a green tea extract powder, a *Gynostemma pentaphyllum* extract
10 powder, and a hawthorn berry extract powder;
(h) combining the green tea extract powder, the *Gynostemma pentaphyllum* extract powder, and the hawthorn berry extract powder in the desired proportions. It is noted that the pooled water extract eluate and the
15 pooled aqueous alcohol extract eluate from each herbal component were dried separately and then the organic residues for that herbal component combined to form the extract powder for that herbal component; or
alternatively, the pooled water extract eluate and the
20 pooled aqueous alcohol extract eluate from each herbal component may be combined and then dried to form the extract powder for that herbal component.

Detailed Description of the Invention

- 25 The present invention relates to a novel herbal extract-based composition that comprises about 10 to about 30 percent by weight of *Gynostemma pentaphyllum* extract, about 10 to about 30 percent by weight of green tea extract, and about 40 to about 75 percent by weight
30 of hawthorn berries extract. Preferably, the herbal extract-based composition comprises about 20 percent by weight of *Gynostemma pentaphyllum* extract, about 20 percent by weight of green tea extract, and about 60 percent by weight of hawthorn berries extract.
35 *Gynostemma pentaphyllum*, *Crataegus pinnatifidia*, and *Camellia sinensis* have been used individually for health

- 6 -

promoting and therapeutic purposes. However, the herbal extract-based composition of the present invention is an arrangement and unique combination that has been found to provide previously unknown therapeutic or health promoting benefits. More particularly, the herbal extract-based composition, in a pharmacologically effective amount and regimen, can reduce the effects of aging such as the formation of brown spots; increases metabolism for elimination of lactate; reduces body weight, increases alertness; improves oxygen uptake for physical and mental performance; increases physical endurance; increases tolerance of oxygen deprivation; rejuvenates skin; reduces alcohol induced liver injury; improves red cell deformability; reduces plasma fibrinogen; inhibits thrombus formation; relieves constipation; reduces halitosis; inhibits oxidation of unsaturated fatty acids thereby suppressing undesirable body odor; helps to prevent the formation of cataracts; helps to prevent hyperglycemia; inhibits the breakdown of collagen by free radicals (thereby decreasing the manifestations of autoimmune diseases such as rheumatoid arthritis, scleroderma, and other collagen diseases); aids to detoxify the body from heavy metals (because of the ability of the composition to absorb and precipitate lead, mercury, nickel, chromium, silver and copper ions); aids to detoxify the body from alcohol (because of the ability of the composition to combine with alkaloids and act to neutralize toxicity and accelerate the elimination of alcohol through the urinary and gastrointestinal systems); aids to prevent formation, and to reduce the size if formed, of gallstones and lithiasis from the urinary tract; aids to inhibit or reduce prostate cancer cell growth and prostate hyperplasia; reduces reperfusion injury (by neutralizing free radicals and by lessening calcium accumulation in the myocardium and reducing plasma lactate dehydrogenase

and creatine phosphokinase levels); aids to reverse memory impairment caused by drugs (e.g., alcohol, pentobarbital), reduces the frequency and severity of cerebral transient ischemia attacks, and shows a broader spectrum of anti-microbial activity than reported for green tea alone. Additional health promoting benefits that have been previously described as intrinsic to the separate components of the combination, and thus to the combination itself, include the benefits of inhibiting platelet aggregation; inhibiting the formation of dental plaque by inhibiting the growth of *Streptococcus mutans* (implicated in the formation of dental caries); and aiding in reducing the onset of certain forms of cancer, atherosclerotic heart disease, diabetes, and hypertension.

Depending on the desired use of the herbal extract-based composition according to the present invention to provide one or more particular health promoting and/or therapeutic effects, the composition can be provided as the main pharmacologically active components in a form including, but not limited to, a tea, a liquid extract, a beverage, a gum, a lozenge, a tablet (including capsule), or a topical agent. In one embodiment, the composition is included in a chewing gum formulation. The composition of chewing gum is conventional, and well known to those skilled in the art. For example, a gum base that may be mixed with the composition includes a base comprised of arabic, guar, natural rubber gums; sweeteners (sugar, stevia, saccharin, sorbitol, aspartame); flavoring agents (e.g., mints, fruits), coloring agents; or a combination thereof. In another embodiment, the composition is used as a tea.

In another embodiment, the composition is included in a beverage formulation. The composition of beverages are conventional, and well known to those skilled in the art. For example, an aqueous carrier that may be mixed

with the composition includes carriers comprised of spring water, filtered water, distilled water, carbonated water, juices, or combinations thereof. Additionally, the beverage may further comprise components known to the beverage industry including preservative agents, sweeteners, flavoring agents, coloring agents, and combinations thereof.

In another embodiment, the composition is in extract form. The composition of herbal extracts are conventional, and well known to those skilled in the art. For example, an aqueous carrier that may be mixed with the composition includes carriers comprised of spring water, filtered water, or distilled water. Additionally, the extract may further comprise components including preservative agents, sweeteners, flavoring agents, coloring agents, and combinations thereof.

In another embodiment, where topical application to the skin or mucous membranes is desired to provide health promoting effects, the composition may be incorporated into a cream or ointment base. Suitable bases are known to those skilled in the art to include one or more of purified water, lanolin, propylene glycol, mineral oil, vegetable or flower oils, glycerin, glyceryl stearate, cetyl alcohol, propylparaben, preservatives, fragrance and the like. Formulations containing the herbal extract-based composition according to the present invention may comprise topical agents including, but not limited, to a rinse, a cream, an ointment, a gel, and a suppository. It will be appreciated by those skilled in the art that the pharmacological effective concentration of the herbal extract-based composition in the formulation will depend on other ingredients in the formulation, the mode of administration of the formulation, the physiologic site

to be treated, and the desired health promoting or therapeutic effect to be provided.

In another embodiment, the composition may be incorporated into a tablet (including capsule, caplet, and the like). Suitable bases are known to those skilled in the art to include fillers, binders, coatings, excipients and combinations thereof. For example, base ingredients include, but are not limited to, plant cellulose, natural silica, magnesium stearate, wax, vegetable glycerides, vegetable stearate, and a combination thereof.

The therapeutic and/or health promoting benefits provided by the arrangement and unique combination of Gynostemma pentaphyllum extract, green tea extract, and hawthorn berries extract comprising the herbal extract-based composition of the present invention may be more apparent by the following examples which are provided for purposes of illustration, and not limitation.

EXAMPLE 1

In this embodiment is illustrated a process for preparing the herbal based-extract of the present invention. In this process of preparation, selectively extracted from each component herb are compounds (some yet to be chemically defined) with particular types of pharmacological activities. Using this process results in extracts that contain high concentrations of pharmacologically active compounds which comprise the active ingredients in the herbal extract-based composition of the present invention. The extraction process of the present invention selectively extracts target compounds of desired pharmacological activity, and thus, the extraction process should not be considered a "traditional extraction"; and the resultant extract is more appropriately viewed as a selective concentration of a combination of pharmacologically

active components rather than a "total extract". Thus, using the method according to the present invention is an approach to control the quality of, and standardize the composition of the target compounds to be
5 selectively extracted for, the herbal extract-based composition of the present invention.

The method according to the present invention comprises separately extracting each of hawthorn berries (or leaves), green tea leaves, and Gynostemma
10 pentaphyllum; drying extraction eluates obtained from the extracting of each of hawthorn berries, green tea leaves, and Gynostemma pentaphyllum leaves to obtain organic residues in forming a hawthorn berry extract powder, green tea extract powder, and a Gynostemma
15 pentaphyllum extract powder; and combining the green tea extract powder, the Gynostemma pentaphyllum extract powder, and the hawthorn berry extract powder in desired proportions to form the herbal extract-based composition. In one embodiment of the present
20 invention, the method comprises the steps of:
(a) separately extract a first batch of macerated hawthorn berries, cut green tea leaves, and cut Gynostemma pentaphyllum leaves ("the herbal components") in warm (greater than room temperature) water;
25 (b) recovering a first extraction eluate from the respective extraction of each herbal component;
(c) re-extracting each herbal component by repeating step (a), recovering a second extraction eluate, and pooling the second extraction eluate with the first
30 extraction eluate of the respective herbal component;
(d) separately extracting a second batch of macerated hawthorn berries, cut green tea leaves, and cut Gynostemma pentaphyllum leaves in an aqueous alcohol (e.g., 70% ethanol);

- 11 -

- (e) recovering a first aqueous alcohol extraction eluate from extracting the second batch of each herbal component;
- (f) re-extracting the second batch of each herbal component by repeating step (d), recovering a second aqueous alcohol extraction eluate, and pooling the second aqueous alcohol extraction eluate with the first aqueous alcohol extraction eluate of the respective herbal component;
- (g) recovering the organic residue from each of the pooled extraction eluates by reducing the liquid portion of each of the pooled extraction eluates by drying (air drying, freeze drying, or a combination thereof) in forming a green tea extract powder, a Gynostemma pentaphyllum extract powder, and a hawthorn berry powder;
- (h) combining the green tea extract powder, the Gynostemma pentaphyllum extract powder, and the hawthorn berry extract powder in the desired proportions.
- In a preferred embodiment, the process for making the herbal extract-based composition comprises the steps of:
- (a) macerating hawthorn berries, and cutting the green tea leaves and cutting the Gynostemma pentaphyllum leaves into small pieces (e.g., millimeter size) while keeping the three components separate;
- (b) placing the macerated hawthorn berries, cut green tea leaves, and cut Gynostemma pentaphyllum leaves ("the herbal components") into separate containers;
- (c) separately diluting each herbal component in warm water, preferably at in a temperature range of between approximately 70EC to 80EC, preferably in a ratio range of water to each herbal component of five to one;
- (d) allowing each herbal component to soak in the warm water for at least 1 hour (preferably for 2-4 hours);

- 12 -

- (e) collecting an extraction eluate from each soaking of the herbal components into separate receptacles;
- (f) re-extracting the macerated hawthorn berries, cut green tea leaves, and cut Gynostemma pentaphyllum leaves in a warm solution of water by repeating steps (c)-(d);
- 5 (g) collecting a re-extraction eluate from each re-extraction of each of the herbal components and pooling the re-extraction eluate with the extraction eluate of the respective herbal component; and in an extraction of
- 10 a second batch of macerated hawthorn berries, cut green tea leaves, and cut Gynostemma pentaphyllum leaves in an aqueous alcohol;
- (h) placing the second batch of macerated hawthorn berries, cut green tea leaves, and cut Gynostemma
- 15 pentaphyllum leaves ("the herbal components") into separate containers;
- (i) separately diluting each herbal component in an aqueous alcohol solution (preferably, 70% ethanol; preferably at room temperature, e.g., a range of between
- 20 approximately 25EC to 40EC; preferably in a ratio range of alcohol solution to each herbal component of five to one);
- (j) allowing each herbal component to soak in the aqueous alcohol solution for at least 1 hour (preferably
- 25 for 2-4 hours);
- (k) collecting the aqueous alcohol solution extraction eluate from the soaking of each of the herbal components into separate receptacles;
- (l) re-extracting the second batch of macerated hawthorn
- 30 berries, cut green tea leaves, and cut Gynostemma pentaphyllum leaves in an aqueous alcohol solution by repeating steps (i)-(j);
- (m) collecting the aqueous alcohol solution re-extraction eluates from the soaking of each of the
- 35 herbal components and pooling each aqueous alcohol solution supernatant re-extract with the aqueous alcohol

solution extraction eluate of the respective herbal component;

(n) recovering the organic residue from the pooled aqueous alcohol extraction eluate of each herbal component by reducing the liquid portion of each of the
5 respective pooled aqueous alcohol extraction eluate by drying (air drying, freeze drying, or a combination thereof) in forming a green tea extract powder, a Gynostemma pentaphyllum extract powder, and a hawthorn
10 berry extract powder; and
(o) combining the green tea extract powder, the Gynostemma pentaphyllum extract powder, and the hawthorn berry extract powder in the desired proportions to form a herbal extract based composition.

15 In illustrating a preferred embodiment, and following the process for producing the herbal extract-based composition, the herbal extract-based composition may be formed by mixing about 10 to about 30 percent by weight of Gynostemma pentaphyllum extract powder, about
20 10 to about 30 percent by weight of green tea extract powder, and about 40 to about 75 percent by weight of hawthorn berries extract powder. In a more preferred embodiment, the herbal extract-based composition comprises about 20 percent by weight of Gynostemma
25 pentaphyllum extract powder, about 20 percent by weight of green tea extract powder, and about 60 percent by weight of hawthorn berries extract powder. Continuing this illustration of a preferred embodiment, the herbal extract-based composition is formed into a caplet,
30 wherein the Gynostemma pentaphyllum extract powder, green tea extract powder, hawthorn berries extract powder comprise 500mg. In such caplet form, and intrinsic to the herbal extract-based composition is typically found at least 75 mg (or at least 15% by
35 weight) of proanthocyanidins, at least 75 mg (or at least 15% by weight) saponins (e.g., gypenosides) and at

- 14 -

least 75 mg (or at least 15% by weight) green tea polyphenols. In such caplet form, a preferred dosage and regimen for an adult male or female to effect the health promoting and/or therapeutic effects provided by the herbal extract-based composition of the present invention is 1 caplet, three times daily; and preferably shortly before meals.

EXAMPLE 2

In this embodiment is illustrated a use of the herbal extract-based composition of the present invention. In this illustration, 20 post-thrombotic stroke in-patients (mean age 59 ± 6 ; 16 males, 4 females) with hemiparesis and/or focal neurological deficits of mild to moderate degree of severity took the caplet dosage and regimen illustrated above for a period of at least 30 days, in addition to any standard symptomatic therapy. After the 30 day period, patients taking the herbal extract-based composition, as compared to the control group of patients not taking the herbal extract-based composition, showed significant improvement. The significant improvement in the treated group comprised improved alertness, cognition with quicker response; improved memory function, particularly for recall of recent events; improved numerical calculation; reduction of drowsiness and dizziness; reduction of anxiety and depression; and increased energy and vitality. Additionally, the patients treated with the herbal extract-based composition according to the present invention showed a statistically significant reduction in body weight of $1.41 \text{ kg} \pm 0.56$ (standard deviation; $P < 0.05$); a statistically significant reduction of abdominal circumference of $1.76 \text{ cm} \pm 0.56$ ($P < 0.01$); a decreased blood viscosity, a decrease in cholesterol of $20 \text{ mg} \pm 5$ (standard deviation), a decrease in serum triglycerides of $28.6 \text{ mg} \pm 7.8$, and a statistically

significant decrease in fibrinogen of $88.6\text{mg} \pm 9.1$ ($P < 0.05$), as compared to the respective measurement before treatment was initiated.

5

EXAMPLE 3

In this embodiment is illustrated the use of the herbal extract-based composition of the present invention. In this illustration, treated with the caplet form (as described in Example 1) were six
10 patients (mean age 56) suffering from transient ischemia attacks, cerebrovascular spasm, and several cases of multiple lacunar cerebral infarction with a long-standing history of hypertension. After treatment for at least 30 days, the patients showed improved general
15 conditions including improved memory, increased mental awareness, decreased vertigo and dizziness, a reduction in fatigue, increased physical endurance and improved fine motor coordination, a reduction of facial muscular weakness, and a cessation of transient ischemia attacks.
20 Additionally, the patients treated with the herbal extract-based composition according to the present invention showed a statistically significant reduction in body weight of $1.41\text{ kg} \pm 0.56$ (standard deviation; $P < 0.05$); a statistically significant reduction of
25 abdominal circumference of $1.76\text{ cm} \pm 0.56$ ($P < 0.01$); a decreased blood viscosity, a decrease in cholesterol of $20\text{mg} \pm 5$ (standard deviation), a decrease in serum triglycerides of $28.6\text{mg} \pm 7.8$, and a statistically significant decrease in fibrinogen of $88.6\text{mg} \pm 9.1$
30 ($P < 0.05$), as compared to the respective measurement before treatment was initiated.

In another illustration of the health promoting effects by providing a reduction in fatigue, 1 group of mice was treated with the herbal extract-based
35 composition according to the present invention using 60 mg/day (delivered by gastric tube) for 14 days. A

- 16 -

control group of mice remained untreated. It is known that prolonged physical exertion, exercise, and prolonged mental concentration can generate an excess of lactate within the body; and that lactate release is a major cause of muscle fatigue (see, e.g., Hogan et al., *J. Appl. Physiol.* 65:815). As shown in Table 1, it was found treating mice with the herbal extract-based composition of the present invention (denoted "HEBC"), followed by an forced exercise regimen for seven hours, can speed up body metabolism for the elimination of lactate (43% reduction in serum lactic acid levels), as compared to the control group of mice (denoted "control"). Hence, in the treated group is a more rapid recovery from fatigue, resulting in increased physical and mental endurance as compared to the controls.

Table 1

mice	Lactic acid (mg) before exercise	Lactic acid (mg) after exercise
control	250.0 \pm 40.4	712.5 \pm 25.3
HEBC-treated	250.0 \pm 40.0	425.6 \pm 65.2

In a further illustration of health promoting effects of the herbal extract-based composition according to the present invention, the composition was tested for anti-stress activity (effecting increased physical endurance) using the "mice swimming endurance test" (Grandhi et al., 1994, *J. Ethnopharmacol.* 44:131). A control group of 15 mice, a group of 15 mice treated with the herbal extract-based composition at a dosage of 60 mg/day for 14 days ("group 2"), and a group of 15 mice treated with the herbal extract-based composition at a dosage of 120 mg/day for 14 days ("group 3") were evaluated for swimming time in this assay. As shown in Table 2, a statistically significant increase in swimming time was shown in the mice treated

with the herbal extract-based composition (groups 2 and 3; $P < 0.05$) as compared to the control group.

Table 2

mice	swim time (minutes) \pm std. dev.
control	13.79 \pm 7.85
group 2	22.85 \pm 11.08
group 3	24.68 \pm 13.49

EXAMPLE 4

In this embodiment is illustrated the use of the herbal extract-based composition of the present invention. In this illustration, treated with the caplet form (as described in Example 1) were 80 obese patients and patients with hyper-lipidemia. After treatment for at least 30 days, the patients showed an average reduction of body weight of 2.0 kg and a reduction in the levels of both serum triglyceride and cholesterol of 20%, as compared to pre-treatment measurements. Additionally, there was increased vitality, a sense of well-being, and improved skin appearance among the treated patients. For male patients, there was a reduction in the urinary frequency and nocturia, with palpable reduction of prostate size.

Improvement in skin appearance, as observed by a reduction and disappearance of acne, was also observed in a study of young individuals suffering from acne. Treatment of such individuals with the herbal extract-based composition according to the present invention was effective in reducing acne with a treatment period of at least 30 days. Other benefits to the skin observed in individuals using the herbal extract-based composition include a decreased pigmentation of senile freckles. In another illustration of health promoting effects provided by the herbal extract-based composition

according to the present invention, the composition was tested for its ability to reduce malondialdehyde (MDA) in the serum of treated animals. A known breakdown product of lipid peroxides in aging skin is MDA. MDA has been shown to cross-link with collagen, which is one mechanism by which the elasticity of skin decreases with age.

A control group of 10 mice, and a group of 10 mice treated with the herbal extract-based composition (by gastric tube- 60 mg/day for 14 days; group 2) were evaluated for the ability to reduce the formation of MDA. As shown in Table 3, group 2 demonstrated a statistically significant decrease in MDA as compared to the control group.

Table 3

mice	MDA :mol/ml \pm std. dev.	% change from control
control	1.201 \pm 0.12	----
group 2	0.923 \pm 0.15	- 20.2

EXAMPLE 5

In this embodiment, the health promoting effects of the herbal extract-based composition according to the present invention are further illustrated. Ten patients (mean age 56 \pm 4.3; 7 males, 3 females) with severe coronary atherosclerosis and varying degrees of myocardial ischemia began taking the caplet form (as described in Example 1) for at least 30 days. Following the treatment period, the patients showed reductions in frequencies and intensities of angina and tachycardia, decreased anxiety and depression, an improved sense of well being, improved EKG tracings with decreased arrhythmia, and decreases in serum cholesterol levels (15mg/dl \pm 4) and triglyceride levels (50mg/dl \pm 8.4),

and a decrease in the level of plasma fibrinogen (150mg/dl \pm 21).

EXAMPLE 6

5 In this embodiment, the health promoting effects of the herbal extract-based composition according to the present invention are further illustrated. Radiation (e.g., ^{60}Co) can induce cytogenic damage in leukocytes resulting in more leukocytes with micronuclei
10 in the peripheral circulation. Thus, peripheral leukocytes with micronuclei in individuals may be used as an index to cytogenic damage induced by radiation exposure. Sixty patients (30 male, 30 female, mean age 52 years) with an advanced stage of a malignant tumor
15 received standard radiation therapy. In 97% of the patients receiving the herbal extract-based composition according to the present invention (caplet form, as described in Example 1), leukopenia was reduced (e.g., by as much as about 50%) following radiation therapy.

20 To further illustrate the protection of leukocytes from radiation damage and killing, a control group of 10 mice were untreated and not exposed to radiation. A second group of control mice were untreated and then exposed to a standard dose (300 rads) of ^{60}Co (group 2).
25 A third group of mice was treated with 300 mg/kg of body weight/day of the herbal extract-based composition according to the present invention (by gastric tube, and for 10 days), and exposed to a standard dose of ^{60}Co (group 3). A fourth group of mice was treated with 400
30 mg/kg of body weight/day of the herbal extract-based composition according to the present invention (by gastric tube, and for 10 days), and exposed to a standard dose of ^{60}Co (group 4). As shown in Table 4, there were statistically significant reductions in
35 micro-nucleus formation and leukopenia (as measured by the number of white blood cells/mm) in the mice treated

with the herbal extract-based composition as compared to group 2 (untreated, irradiated).

Table 4

5

10

mice	WBC/mm \pm std. dev.	Change (%)	Micronucleus (%)
control	7000 \pm 550	---	2.3
group 2	1910 \pm 450	-72.7	17.6
group 3	4110 \pm 4331	+115.2	4.0
group 4	4500 \pm 4701	+135.2	2.1

From the foregoing, it will be obvious to those skilled in the art that various modifications in the above-described methods, and compositions can be made without departing from the spirit and scope of the invention. Accordingly, the invention may be embodied in other specific forms without departing from the spirit or essential characteristics thereof. Present embodiments and examples, therefore, are to be considered in all respects as illustrative and not restrictive, and all changes which come within the meaning and range of equivalency of the claims are therefore intended to be embraced therein.

- 21 -

What is claimed is:

1. An herbal extract-based composition comprising an extract of *Gynostemma pentaphyllum*, an extract of
5 *Crataegus pinnatifidia* (hawthorn), and an extract of *Camellia sinensis* (green tea).
2. The herbal extract-based composition according to claim 1, wherein the herbal extract-based composition
10 comprises about 10 to about 30 percent by weight of *Gynostemma pentaphyllum* extract, about 10 to about 30 percent by weight of green tea extract, and about 40 to about 75 percent by weight of hawthorn berries extract
- 15 3. The herbal extract-based composition according to claim 1, wherein the herbal extract-based composition comprises about 20 percent by weight of *Gynostemma pentaphyllum* extract, about 20 percent by weight of green tea extract, and about 60 percent by weight of
20 hawthorn berries extract.
4. The herbal extract-based composition according to claim 1, further comprising a gum base in forming a chewing gum formulation.
25
5. The herbal extract-based composition according to claim 1, wherein the gum base is selected from the group consisting of arabic, guar, natural rubber gum, sweetener, flavoring agent, coloring agent, and a
30 combination thereof.
6. The herbal extract-based composition according to claim 1, further comprising an aqueous carrier in forming a beverage formulation.
35

7. The herbal extract-based composition according to claim 6, wherein the aqueous carrier is selected from the group consisting of spring water, filtered water, distilled water, carbonated water, juices, and a combination thereof.

8. The herbal extract-based composition according to claim 1, further comprising an aqueous carrier in forming an extract formulation.

9. The herbal extract-based composition according to claim 8, wherein the aqueous carrier is selected from the group consisting of spring water, filtered water, and distilled water.

10. The herbal extract-based composition according to claim 9, further comprising a component selected from the group consisting of a preservative agent, sweetener, flavoring agent, coloring agent, and a combination thereof.

11. The herbal extract-based composition according to claim 1, further comprising a cream or ointment base in forming a topical formulation.

12. The herbal extract-based composition according to claim 8, wherein the cream or ointment base is selected from the group consisting of purified water, lanolin, propylene glycol, mineral oil, vegetable or flower oils, glycerin, glyceryl stearate, cetyl alcohol, propylparaben, preservatives, fragrance, and a combination thereof.

13. The herbal extract-based composition according to claim 1, further comprising a base in forming a tablet formulation.

14. The herbal extract-based composition according to claim 13, wherein the base is selected from the group consisting of a filler, binder, coating, excipients, and a combination thereof.

5

15. The herbal extract-based composition according to claim 13, wherein the base is selected from the group consisting of plant cellulose, natural silica, magnesium stearate, wax, vegetable glycerides, vegetable stearate, and a combination thereof.

10

16. A process for preparing a herbal extract-based composition comprising separately extracting each of hawthorn berries or leaves, green tea leaves, and Gynostemma pentaphyllum leaves; drying extraction eluates obtained from the extracting of each of hawthorn berries or leaves, green tea leaves, and Gynostemma pentaphyllum leaves to obtain organic residues in forming a hawthorn extract powder, green tea extract powder, and a Gynostemma pentaphyllum extract powder; and combining the green tea extract powder, the Gynostemma pentaphyllum extract powder, and the hawthorn extract powder in desired proportions to form the herbal extract-based composition.

15

20

25

17. A process for preparing a herbal extract-based composition comprising the steps of:

(a) separately extracting a first batch of each of three herbal components, wherein the components are macerated hawthorn berries, cut green tea leaves, and cut Gynostemma pentaphyllum leaves, in warm water;

30

(b) recovering a first extraction eluate from the respective extraction of each herbal component;

(c) re-extracting each herbal component by repeating step (a), recovering a second extraction eluate, and

35

pooling the second extraction eluate with the first extraction eluate of the respective herbal component;

(d) separately extracting a second batch of each of three herbal components, wherein the components are
5 macerated hawthorn berries, cut green tea leaves, and cut *Gynostemma pentaphyllum* leaves, in an aqueous alcohol;

(e) recovering a first aqueous alcohol extraction eluate from extracting the second batch of each herbal
10 component;

(f) re-extracting the second batch of each herbal component by repeating step (d), recovering a second aqueous alcohol extraction eluate, and pooling the second aqueous alcohol extraction eluate with the first
15 aqueous alcohol extraction eluate of the respective herbal component;

(g) recovering the organic residue from each of the pooled extraction eluates by reducing the liquid portion of each of the pooled extraction eluates by drying, in
20 forming a green tea extract powder, a *Gynostemma pentaphyllum* extract powder, and a hawthorn berry powder;

(h) combining the green tea extract powder, the *Gynostemma pentaphyllum* extract powder, and the hawthorn
25 berry extract powder in desired proportions in forming the herbal extract-based composition.

18. The process according to claim 17, wherein the water of step (a) is in a temperature range of from 70EC
30 to 80EC, and in a ratio to each herbal component of 5:1, and is in contact with each herbal component for at least one hour.

19. The process according to claim 18, wherein the
35 water is in contact with each herbal component for a time in a range of 2 to 4 hours.

20. The process according to claim 17, wherein the aqueous alcohol is 70% ethanol at room temperature.

21. The process according to claim 17, wherein the
5 drying in step (g) is a process selected from the group consisting of air drying, freeze-drying, and a combination thereof.

22. A process for preparing a herbal extract-based
10 composition comprising the steps of:

- (a) separately preparing three herbal components by macerating hawthorn berries, cutting green tea leaves and cutting leaves of Gynostemma pentaphyllum into small pieces;
- 15 (b) placing the macerated hawthorn berries, cut green tea leaves, and cut Gynostemma pentaphyllum leaves into separate containers;
- (c) separately diluting each herbal component in warm water, wherein the water is in a temperature range of
20 between approximately 70EC to 80EC and in a ratio of water to each herbal component of five to one;
- (d) allowing each herbal component to soak in the warm water for at least 1 hour;
- (e) collecting an extraction eluate from each soaking of
25 the herbal components into separate receptacles;
- (f) re-extracting the macerated hawthorn berries, cut green tea leaves, and cut Gynostemma pentaphyllum leaves in a warm solution of water by repeating steps (c)-(d);
- (g) collecting a re-extraction eluate from each re-
30 extraction of each of the herbal components and pooling the re-extraction eluate with the extraction eluate of the respective herbal component; and in an extraction of a second batch of macerated hawthorn berries, cut green tea leaves, and cut Gynostemma pentaphyllum leaves in an
35 aqueous alcohol;

- 26 -

- (h) placing the second batch of macerated hawthorn berries, cut green tea leaves, and cut Gynostemma pentaphyllum leaves into separate containers;
- (i) separately diluting each herbal component in the
5 second batch in an aqueous alcohol solution;
- (j) allowing each herbal component to soak in the aqueous alcohol solution for at least 1 hour;
- (k) collecting the aqueous alcohol solution extraction eluate from the soaking of each of the herbal components
10 into separate receptacles;
- (l) re-extracting the second batch of macerated hawthorn berries, cut green tea leaves, and cut Gynostemma pentaphyllum leaves in an aqueous alcohol solution by repeating steps (i)-(j);
- (m) collecting the aqueous alcohol solution re-
15 extraction eluates from the soaking of each of the herbal components and pooling each aqueous alcohol solution supernatant re-extract with the aqueous alcohol solution extraction eluate of the respective herbal
20 component;
- (n) recovering the organic residue from the pooled aqueous alcohol extraction eluate of each herbal component by reducing the liquid portion of each of the respective pooled aqueous alcohol extraction eluate by
25 drying in forming a green tea extract powder, a Gynostemma pentaphyllum extract powder, and a hawthorn berry extract powder; and
- (o) combining the green tea extract powder, the Gynostemma pentaphyllum extract powder, and the hawthorn
30 berry extract powder in desired proportions to form a herbal extract based composition.

23. The process according to claim 22, wherein the
water is in contact with each herbal component for a
35 time in a range of 2 to 4 hours.

24. The process according to claim 22, wherein the aqueous alcohol is 70% ethanol.

25. The process according to claim 22, wherein the
5 aqueous alcohol is in contact with each herbal component for a time in a range of 2 to 4 hours.

26. The process according to claim 22, wherein the
drying in step (n) is a process selected from the group
10 consisting of air drying, freeze-drying, and a combination thereof.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US98/05494

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :AOIN 65/00

US CL :424/195.1

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/195.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

APS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5,362,494 A (ZYSMAN et al) 08 November 1994, see entire document.	1-26

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:	*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
A document defining the general state of the art which is not considered to be of particular relevance	*X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
B earlier document published on or after the international filing date	*Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*A* document member of the same patent family
O document referring to an oral disclosure, use, exhibition or other means	
P document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search 19 JUNE 1998	Date of mailing of the international search report 01 JUL 1998
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer L. BLAINE LANKFORD Telephone No. (703) 308-0196

EUROPEAN PATENT OFFICE

Patent Abstracts of Japan

PUBLICATION NUMBER : 61050907
PUBLICATION DATE : 13-03-86

APPLICATION DATE : 20-08-84
APPLICATION NUMBER : 59172933

APPLICANT : OSAKA CHEM LAB;

INVENTOR : YUCHI SHIGERU;

INT.CL. : A61K 7/00 A61K 35/78 A61K 35/78

TITLE : COSMETIC COMPOSITION CONTAINING EXTRACT OF GYNOSTEMMA
PENETAPHYLLUM MAKINO

ABSTRACT : PURPOSE: To provide a cosmetic composition containing the extract of AMACHA-ZURU (Gynostemma pentaphyllum Makino) as an essential component, having the metabolism-promoting effect to the lipid peroxide of epidermis and the remedying effect of allergic dermatitis, and effective to various dermatic diseases caused by relatively wide range of causes.

CONSTITUTION: The whole grass, leaves and stalks, underground parts, or seeds of AMACHA-ZURU are dried, pulverized, extracted with water or hydrated lower alcohol, and concentrated to obtain an extract. The extract or AMACHA- ZURU saponin prepared by purifying the extract is used as a component of cosmetics such as beauty wash, cream, milky lotion, makeup cosmetic, soap, etc., to obtain a cosmetic composition having the above effect and free from the deterioration of the dermatic disease by the misunderstanding of the cause. The amount of the AMACHA-ZURU saponin to be added to the cosmetic is selected to enable the application of 20~1,000mg of the AMACHA-ZURU saponin daily.

COPYRIGHT: (C)1986,JPO&Japio

THIS PAGE BLANK (USPTO)